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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WANG, CHANG YU	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 01/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,457	ANDERSON ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-35* is/are pending in the application.

4a) Of the above claim(s) *12 and 17-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I and the stem cells of the central nervous system in the reply filed on December 23, 2005 is acknowledged. The traversal is on the ground(s) that the species election of antibody should include anti-P75 and P0 since these two antibodies can be used in combination for cell sorting. It has been fully considered and found persuasive. Therefore, the species election for antibody is withdrawn. The subject matter related to anti-P75 and anti-P0 in the elected Group I will be examined under this office action.

2. Claims 12-35 are pending. Claims 12 and 17-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups II-IV, there being no allowable generic or linking claim. Claims 13-16 are under examination in this office action.

Priority

3. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Information Disclosure Statement

The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for enriching neural crest stem cells from neural crest-derived cells by flow cytometry using anti-P75 and anti-P0 antibodies as selective markers, does not reasonably provide enablement for enriching human neural stem cells from any cell origins as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6. "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

7. The claims are drawn to a method for enriching human neural stem cells comprising selecting cells containing neural stem cells by flow cytometry (FACS) using anti-P75 low affinity neurotrophin receptor (anti-P75) and anti-P0 myelin protein (anti-P0) as selecting markers. The instant specification discloses that neural crest cells derived from embryonic day 14.5 (E14.5) sciatic nerve cells can be enriched by FACS using anti-P75 and anti-P0 antibodies. The fraction of $P75^{+}$ $P0^{-}$ neural crest stem cells was able to continue proliferating and differentiate into neurons and glia cells *in vivo* while transplanted into the sciatic nerve of the animal. However, with limited working examples, Applicant fails to teach whether these selecting protocols and culture conditions can be applied to all types of cells that contain potential neural stem cells or neural precursor cells derived from all different regions of the central nervous systems. In addition, Applicant fails to teach whether all different types of cells or neural precursor cells derived from different cell origins selected with anti-P75 and anti-P0 and cultured with the said condition can still maintain the characteristics of neural stem cells. The embryonic neural tissues for neural culture have not been fully characterized. The control and regulation of cell lineages is still not understood. The embryonic neural tissues contain very diverse cell types including multipotent progenitor cells, restricted neuronal progenitor, and restricted glial progenitor cells (see p. 385, the section of Cell lines derived by oncogene expression, Gottlieb. Annu. Rev. Neurosci. 2002. 25: 381-407). Therefore, it is unpredictable whether the cells derived from embryonic neural

tissues selected with anti-P75 and anti-P0 still have the characteristics of neural stem cells. In addition, Applicant has not discloses what type of cells have the characteristics of neural stem cells after FACS. Furthermore, the cell lineage and characteristics of other cell origins that potentially contain neural stem cells have not been characterized. The phenotypes of each cell type after FACS are different, and each type of cells have the potential to develop into the cell lineage other than neural cells. Thus, whether the cells derived from these different origins still have the potential to maintain the capability of neural stem cells after FACS with anti-P75 and anti-P0 is also unpredictable. The instant specification has not disclosed any information being enabled for enriching human neural stem cells from any cell origins other than neural crest-derived cells. In addition, Applicant has not provided guidance as to whether these different cell origins can continue proliferating and differentiate into functionally active neural cells as broadly claimed. Applicant may be enabled for enriching human neural crest stem cells derived from neural crest-derived cells. However, Applicant has not taught that the cells from different cell origins are able to have the characteristics of the neural stem cells of the central nervous system or even the peripheral nervous system. It would require undue experimentation to first characterize neural cell derived from embryonic neural tissue or cells that potentially contain neural stem cells from different cell origins, then further characterize whether FACS with anti-P75 and anti-P0 can enrich the fraction of neural stem cells while a person of skill in the art at the time uses the invention.

8. Therefore, in view of the lack of guidance in the specification, the unpredictability of inventions, and current status of the prior art, one of skill in the art would be required

to perform undue experimentation in order to practice the claimed invention as it pertains to a method for enriching human neural stem cells comprising selecting cells containing neural stem cells by flow cytometry (FACS) using anti-P75 low affinity neurotrophin receptor (anti-P75) and anti-P0 myelin protein (anti-P0) as selecting markers as broadly claimed. Undue experimentation would indeed be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Obviousness-Type Non-Statutory Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 13-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending

Application No. 10279568. Although the conflicting claims are not identical, they are not patentably distinct from each other because enriching and culturing human neural stem cells by flow cytometery using anti-P75 low affinity neurotrophin receptor and anti-P0 myelin protein antibody as selecting markers in this instant case is the same in view of enriching and isolating neural stem cells using anti-P75 low affinity neurotrophin receptor and anti-P0 antibody as selecting markers as recited in the claims 1-6 of the Application No. 10279568. While the language is not identical, the claims of the instant application and the copending application encompass the same scope of the invention, which claims the same method for enriching and culturing neural stem cells using anti-P75 low affinity neurotrophin receptor and anti-P0 myelin protein as selecting markers. Thus the instant and copending Application claim the same and non-distinct inventions of the method for enriching and culturing neural stem cells.

11. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (U. S. Patent No. 6001654; issued Dec 14, 1999).

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Anderson et al. teach a method for enriching neural crest stem cells from rat neural crest-derived cells by flow cytometry using anti-P75 antibody as a selecting marker (see column 23, lines 34-45). Anderson et al. also teach that neural stem cells can be further characterized by the absence of other surface markers of mature neurons in the PNS, such as myelin protein P0 (see column 8 lines 55-62). Anderson et al. fail to teach using human cells. Anderson et al. further teach that using enriched neural crest stem cells to potentially treat human neurological disorders in the periphery nervous system.

Thus, it would have been obvious for one of ordinary skill in the art at the time of the instant invention was made to incorporate the teachings of Anderson et al. to enrich human neural crest stem cells by flow cytometry using anti-P75 and anti-P0 antibodies. The person of ordinary skill in the art would have been motivated to make those modifications because the cells derived from embryonic neural tissues are heterogenous and contain very diverse cells including multipotent progenitor cells, restricted neuronal progenitor, and restricted glial progenitor cells. The P75 low affinity neurotrophin receptor is expressed in

embryonic neural tissues and highly abundant in neural crest cells. P0 myelin protein 0 is enriched in mature peripheral myelinated schwann cells. One of ordinary skill in the art would have expected success in enriching neural crest stem cells by flow cytometry using anti-P75 and anti-P0 as selecting markers.

Conclusion

NO CLAIM IS ALLOWED.

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

16. Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
January 10, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER